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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/649,547	08/27/2003	Carsten-Peter Carstens	25436/1243	5516

27495 7590 03/27/2007
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EXAMINER

MCGILLEM, LAURA L

ART UNIT	PAPER NUMBER
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1636

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/649,547	Applicant(s) CARSTENS, CARSTEN-PETER	
	Examiner Laura McGillem	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 December 2006.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 4-19 is/are allowed.
- 6) ☒ Claim(s) 1-3 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 February 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

It is noted that claims 11 and 17 have been amended in the response filed 12/28/2006. Claims 1-19 are under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The amendments to claims 11 and 17 overcome the rejections under 35 U.S.C. 112, second paragraph (indefiniteness). The rejection of claims 11 and 17 under 35 U.S.C. 112, second paragraph are withdrawn.

Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is being maintained for reasons of record in the previous Office Action, mailed 6/29/2006 and for reasons outlined below.

Applicant notes that the step of introducing the first and second vectors recited in claim 1 into a prokaryotic host cell which expresses site specific recombinase and Rep protein as required by claim 1, will result in the formation of a product vector which contains a gene of interest, the gene of interest having been transferred from the recited first vector, the gene of interest being interposed between the double-stranded origin of

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replication of the second vector and the site specific recombination site, as well as the other recited characteristics required of the product vector by claim 1.

Applicants submit that the mechanism involved in the *in vivo* formation in a prokaryotic host of the product vector recited in claim 1 involves several steps as described in detail in the specification. First, the site specific, recombinase mediated, recombination of vector 1 and vector 2 at their respective site-specific recombination sites *in vivo* results in the formation of a cointegrate plasmid as described on page 26, third paragraph, as diagrammed in Figure 1, and as described on page 20 of the instant specification. Applicants submit that after the formation of the cointegrate plasmid through site specific, recombinase mediated recombination of vector 1 and vector 2, the cointegrate plasmid then undergoes rolling circle replication initiated by the binding of the Rep protein to a double stranded origin of replication. Applicants submit that rolling circle replication in a typical vector with one double strand origin of replication is described in the final paragraph on page 9 of the specification.

However, the cointegrate plasmid has two double stranded origins of replication- one from vector 1 and one from vector 2. As stated on page 15, last sentence through first two lines of page 16 of the instant specification, a key feature of the present invention ".is that the *in vitro* and *in vivo* replication of a plasmid containing two double stranded origins of replication on the same strand lead to the formation of two smaller plasmids corresponding to the sequences located between the two double stranded origins of replication".

Applicants submit that in the above passage from the specification, "a plasmid containing two double stranded origins of replication on the same strand" is referring to the cointegrate plasmid. And the product vector recited in claim 1 is one "of two smaller plasmids corresponding to the sequences located between the two double stranded origins of replication" of the cointegrate vector. When rolling circle replication of the cointegrate initiates from the double stranded origin of replication adjacent to the single-stranded origin of replication as illustrated in Figure 1, the replication fork proceeds along the template comprising the single-stranded origin of replication, the selectable marker of the second vector (i.e. marker B in Figure 1), and the gene of interest, until it arrives at the next double stranded origin of replication, where an incision is made resulting in the formation of a single stranded circular molecule consisting of the displaced strand, as described on page 28 of the specification. The displaced strand of this single stranded molecule (product vector of claim 1) comprises the single stranded origin of replication of the second vector, the marker of the second vector, the gene of interest and the double stranded origin of replication of the second vector, and the site specific recombination site, but does not include the selectable marker of the first vector, nor the negative selectable marker of the second vector.

In view of the comments above, Applicant submits that the method of claim 1 of introducing the first and second vectors containing the limitations recited in claim 1 into a prokaryotic host cell which expresses site specific recombinase and Rep protein as required by claim 1, will result in the formation of a product vector which contains a gene of interest, as well as the other recited characteristics required of the product

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vector by claim 1, rendering the claimed subject matter particularly pointed out and distinctly claimed.

Applicant's arguments filed 12/28/2006 have been fully considered but they are not persuasive. In the arguments stated above, Applicants have provided explanation of the claimed method as it is presented in the specification. However the indefiniteness of the claimed methods is based on claim 1 as written. Claim 1, lines 5-19 recites the limitation of the first and second vector. Lines 20-27 recite the following:

"wherein said host cell further expresses a gene encoding a Rep protein that can initiate rolling circle replication at said double stranded origins of replication, and wherein said introducing permits formation of a product vector comprising said gene of interest interposed between said double-stranded origin of replication of said second vector and said site-specific recombination recognition site, and wherein said product vector further comprises said single-stranded origin of replication of said second vector and said gene encoding said second selectable marker, said wherein said product vector does not include both of said negative selectable marker and said gene encoding said first selectable marker".

As above, lines 20-21 include the limitation that the host cell expresses a rep protein that can initiate rolling circle replication at said double stranded origins of replication. At this point in the method, the claim describes only the first and second vectors with double stranded origins of replication. Immediately following, the claim includes recitation of the Rep protein that acts on the double stranded origins of replication and followed by the phrase "said introducing permits formation of product vector". Therefore, the skilled artisan is presented with a method comprising the step of introducing a first and second vector, which permits formation of a product vector. As the claim is written, it is not clear how the formation of the product vector is taking place. It is unclear whether the Applicants intend the product vector to be formed by site-specific

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recombination between the two vectors to form a disclosed, but not recited, cointegrate vector which is subject to further steps, or if the product vector should be formed in some other manner.

The "key feature" of the present invention as pointed out *supra* by the Applicants is not clearly presented in the claim. It is unclear on which vector the rep protein acting on in order to initiate rolling circle replication because as the claim is written, only the first and second vectors and the product vector comprise double stranded origins of replication. As discussed in the previous Office action Page 3, as claim 1 is written the functional link between the Rep protein and formation of a product vector from the first and second vector is vague and indefinite.

Conclusion

Claims 4-19 are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura McGillem whose telephone number is (571) 272-8783. The examiner can normally be reached on M-F 8:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Laura McGillem, PhD
Examiner
3/21/2007


REMY YUCEL, PH.D., J.D.
SUPERVISORY PATENT EXAMINER